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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,339	03/12/2004	Masahiro Kakehi	250307US0DIV	6720

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/798,339

Applicant(s)

KAKEHI ET AL.

Examiner

Elizabeth Slobodyansky, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9 and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/891,287.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/12/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a divisional of application 09/891,287 now abandoned.

The preliminary amendment filed concurrently with the application on March 12, 2004 canceling claims 1-8 and adding claims 9 and 10 has been entered.

Claims 9 and 10 are pending.

Claim Objections

Claim 9, with dependent claim 10, is objected to because of the following: Claim 9 recites "the nucleoside 5'-phosphate ester is selected from the group consisting of 5'-inosinic acid and 5'-guanylic acid" (emphasis added). "acid" is not "ester". While the same compound maybe referred to, the use of one term would be appropriate and consistent.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing nucleoside 5'-phosphate ester using *E. coli* in which *ushA* gene and *aphA* gene are mutated or disrupted

resulting in no or decreased 5' nucleotidase activity, does not reasonably provide enablement for a method for producing nucleoside 5'-phosphate ester using *E. coli* in which *ushA* gene and *aphA* gene do not function normally as result of undefined steps and means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

While mutating or disrupting *ushA* gene and *aphA* gene could result in them functioning not normally, there are other possible ways to achieve said result. The specification does not support the broad scope of the claim which encompasses affecting the activity of the genes and their products by undefined steps and means. Those may include antisense nucleotide, various chemical compounds of undisclosed nature that are inhibitors, altering culturing conditions, etc., for example.

Without sufficient guidance, beyond that provided, altering the function of *E. coli* *ushA* gene and *aphA* gene other than by mutating or disrupting said genes resulting in no or decreased activity of the products is unpredictable and the experimentation left to

those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 recite genes that “do not function normally”. What is considered “normally” is defined in the specification by non-limiting examples rendering the claims indefinite (page13, line 18 through page 16, line 24).

Laird et al. (form PTO-1449 filed March 12, 2004, reference AAE) teach an *E. coli* *AphA* is acid phosphatase that exhibits substrate specificity for both 5'- and 3' nucleotides. They teach an *E. coli* *purEK ushA phoA* mutant strain (53H9) lacking periplasmic enzymes with 5'-nucleotidase activity. They further teach an *aphA* deletion derivative of strain 53H9, strain 54G2. They teach that the AphA phosphatase plays an essential role in scavenging 5'-nucleotides.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laird et al.

Laird et al. (form PTO-1449 filed March 12, 2004, reference AAE) teach an *E. coli AphA* is acid phosphatase that exhibits substrate specificity for both 5'- and 3' nucleotides. They teach an *E. coli purEK ushA phoA* mutant strain (53H9) lacking periplasmic enzymes with 5'-nucleotidase activity. They further teach an *aphA* deletion derivative of strain 53H9, strain 54G2. They teach that the AphA phosphatase plays an essential role in scavenging 5'-nucleotides.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce *E. coli* mutants having non-functional, for example, disrupted *ushA* gene and *aphA* gene. The motivation to produce such mutants is provided by Laird et al. who teach 5'-nucleotide dephosphorylating activity of *ushA* gene and *aphA* gene. Mutants with disrupted *ushA* gene and *aphA* gene would have a higher yield of 5'-nucleotides. One of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success because the structures of both *ushA* gene and *aphA* gene were known at the time the invention was made and methods for disrupting known genes were widely used.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thaller et al. alone or in view of Cowman et al.

Thaller et al. (form P7-0-1449 filed March 12, 2004, reference AAB) teach the sequence of the *aphA* gene (page 193, Figure 1). They further characterize 5'-nucleotidase activity of the *E. coli* AphA enzyme (page 195, Table 1). They teach that another 5'-nucleotidase in *E. coli* is UshA (page 197, 2nd column, last paragraph). They suggest producing strains carrying *aphA* mutations (page 198).

Cowman et al. (form PTO-1449 filed March 12, 2004 , reference AAA) teach the *ushA* gene from *E. coli* encoding a 5'-nucleotidase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce *E. coli* mutants having non-functional, for example, disrupted *ushA* gene and *aphA* gene. The motivation to produce such mutants is provided by Thaller et al. who teach 5'-nucleotide dephosphorylating activity of *ushA* gene and *aphA* gene. Mutants with disrupted *ushA* gene and *aphA* gene would have a higher yield of 5'-nucleotides. One of ordinary skill in the art at the time the invention was made would have a reasonable expectation of success because the structures of both *ushA* gene and *aphA* gene were known at the time the invention was made and methods for disrupting known genes were widely used.

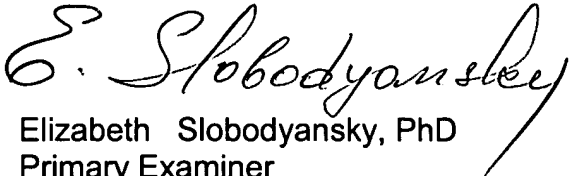
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The

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fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

July 24, 2006